

Finding Creatine nitrate: How Unsafe Supplements Stay on the Market

In November of 2014, I filed a Freedom of Information Act (FOI) Request with the United States Food and Drug Administration. The request was for information about Creatine nitrate, which [the FDA rejected](#) as a [New Dietary Ingredient](#) (NDI), stating that the product would not be reasonably expected to be safe:

For the reasons discussed above, the information in your notification does not provide an adequate basis to conclude that the dietary supplement containing “Creatine Nitrate”, when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Despite this rejection, the product had already been sold as a dietary supplement for several years prior...since the rejection it has been sold for an additional four years. The FDA has known about this and failed to enforce the law, thus leaving a product on the market without reasonable assurance of safety.

Unfortunately for the consumer of Creatine nitrate, nitrate combined with creatine in the body [can form a carcinogen](#):

“...creatine can react with nitrite to form the highly carcinogenic *N*-nitrososarcosine (NSAR)...the toxicological hazard becomes realistic when not only the nitrosation-prone substrate (creatine or protein) but also the nitrosation agent (nitrite) is increased by elevated dietary nitrate consumption above ADI, leading to elevated gastric and circulating nitrite levels...”

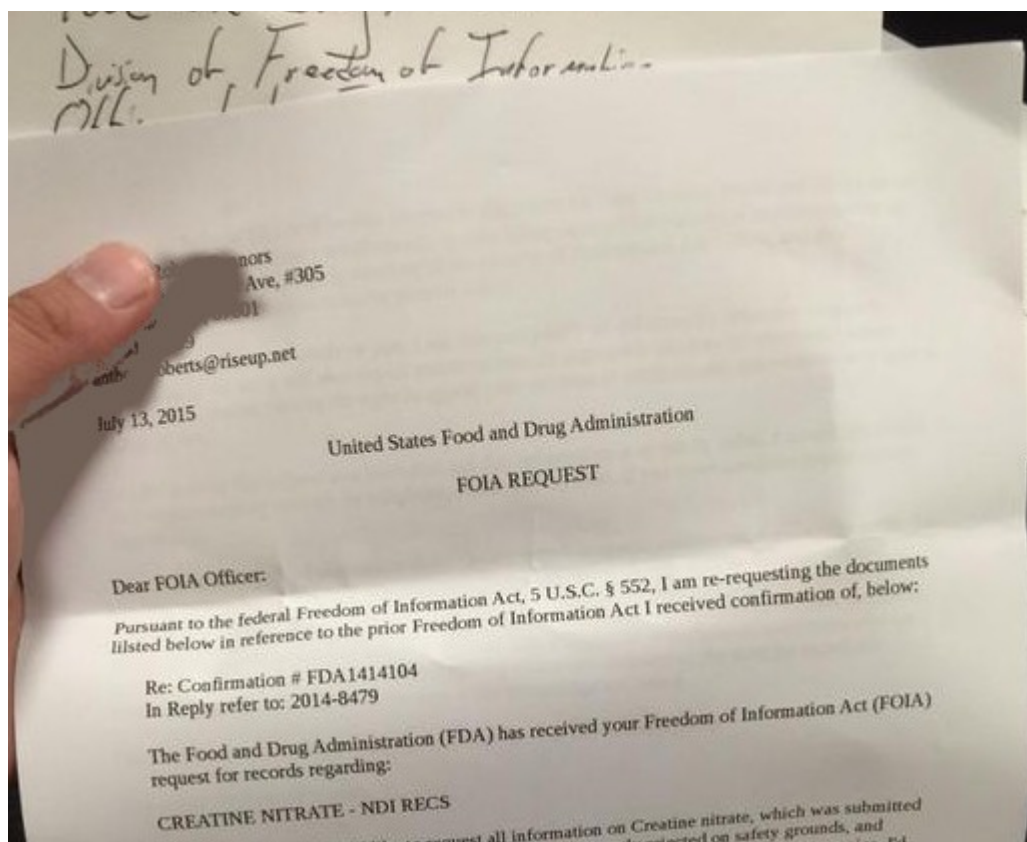
Furthermore, scientists [are warning](#) against the use of nitrate salts for the purposes of increasing performance:

“... at this time we advise athletes to refrain from the uncontrolled use nitrate and nitrite salts as dietary supplements...”

Because I filed my FOI electronically, I received an email that confirmed that my request had been successfully filed. Fast forward eight months to July of 2015, and I still have not received a single document, nor have I received notification that my request is being denied.

After calling the FDA on the phone, and leaving numerous unreturned messages, I finally got a woman on the other line who told me that sometimes electronic FOI requests aren't processed (at all). Because the FDA's national headquarters is within half a day's drive from me, I informed her of my intent to drive there immediately and make use of the “reading room” to find the documents I required. She told me that this wasn't an option, since the FDA had “gone green,” and no longer had a reading room for this purpose.

I was forced to resubmit a FOI request that had already been submitted over half a year earlier.



NDI vs/ GRAS

When an ingredient has not previously been found in food, a NDI notification must be filed with the FDA. During the NDI submission period, the applicant submits paperwork for his or her ingredient to be used as a new dietary ingredient. The FDA then has 75 days to respond—no response is to be interpreted as they do not object to the ingredient. A response (as seen in the excerpt above) will generally state a reason for the ingredient being prohibited for sale.

For ingredients that occur in the food chain, but have not previously been used in dietary supplements, a manufacturer can self-affirm it to be Generally Regarded as Safe (GRAS). However, this does not apply to Creatine nitrate, and [the FDA has been quite clear that self-affirmed GRAS is not a way to get around the NDI requirement and approval process](#). Despite the fact that this does not apply to the ingredient in question, [the patent-holder nevertheless self-declared GRAS](#).

However, even more telling than the GRAS declaration itself, is the fact that the press release from the patent-holder seems to imply that GRAS status was granted—when the truth is that it was “granted” by “experts” that were hired by the company specifically to “grant” the status—which is simply self-declaration of GRAS, as *the panel of experts have no legislative or legal authority to grant anything*.

Nothing.

It’s also worth noting that the patent-holder’s own press release has cited the safe dose as

1,570mgs/day:

ThermoLife International, LLC Announces Issuance of GRAS Status for Creatine Nitrate

A panel of internationally renowned experts, has granted GRAS (Generally Recognized As Safe) Status to ThermoLife International's patented ingredient, Creatine nitrate.

PHOENIX, AZ (PRWEB) JUNE 18, 2012

ThermoLife International, LLC (ThermoLife) announced today that their patented and novel form of creatine, Creatine nitrate was granted GRAS Status on May 23rd, 2012

ThermoLife is proud to announce that an Expert Panel of internationally renowned experts, including Senior Toxicologist Claire Kruger (Spherix Inc.), and IFT President Roger Clemens (ift.org), was convened to perform a comprehensive and critical review of available information and data on the safety of Creatine nitrate and has concluded that Creatine nitrate is Generally Recognized As Safe (GRAS) for use in food, and satisfies all regulatory requirements for use as a dietary supplement.



The expert panel concluded that Creatine nitrate is Generally Recognized As Safe (GRAS) at a dose of 1,570mg per day, every single day for a lifetime of use.”

Therefore, Creatine nitrate is prohibited for sale, in no uncertain terms, per the FDA response to the NDI application—even in light of the self-declared GRAS attempt. Regardless of this fact, it is currently sold at places like Vitamin Shoppe, GNC, and Bodybuilding.com, and it is sold by companies like MusclePharm, Cellucor, and many others...and often, it is sold with a daily dose that exceeds the manufacturer's own safety threshold. It's one of the most popular and expensive forms of creatine, and with millions being made each month, these companies are willing to overlook the fact that it may be cancerous.

Universities, Scientists, and Journals: Willing Accomplices

Back in 2011, around the same time as the FDA was rejecting Creatine nitrate, The University of Oklahoma was in the midst of performing a study on it. Let's put this in no uncertain terms: **The University of Oklahoma was testing a dietary ingredient that lacked NDI approval on subjects who did not know this to be the case.** That study, funded by the patent-holder ([a convicted felon](#)) was ultimately cancelled for [numerous protocol violations](#) and the professor in charge of the study was [allowed to resign](#), but can not work for the University in any capacity in the future.

After the study was cancelled, the professor (Chad Kerksick) sent an email to the patent-holder (Ron Kramer), promising that he'd get the study completed by "Rick."

RE: Studies

Subject: RE: Studies
From: "Ron Kramer" [REDACTED]
Date: Mon, 16 May 2011 10:21:37 -0700
To: "Chad Kerkick, PhD" [REDACTED]

Can you send me Dib's head in a box please? If not both his thumbs will do.

Thanks!!!

From: Chad Kerkick, PhD [REDACTED]
Sent: Monday, May 16, 2011 10:16 AM
To: Ron Kramer
Subject: Re: Studies

I will do what I can for you to make it right.

On Mon, May 16, 2011 at 11:59 AM, Ron Kramer [REDACTED] wrote:
Great. I appreciate your assistance in this fiasco.

Thanks!!

From: Chad Kerkick, PhD [REDACTED]
Sent: Monday, May 16, 2011 9:58 AM
To: [REDACTED]
Subject: Studies

I already contacted Rick this morning and gave him a tentative budget and outlines of the studies. He said they should be able to do them. I'm working on developing the grant proposal into his format to save him time so we can work faster.

He'll need a basic letter of commitment to doing the studies. I will provide an example later today and put you guys in contact.

Chad

Rick is Dr. Richard Kreider of Texas A&M

By 2014, we find Kreider's name on [a study](#) that examined a multi-ingredient product that included 2 grams of Creatine nitrate. That study became a poster presentation for the ISSN, the International Society of Sports Nutrition, and published by their journal. Kreider is listed as an Editor-in-Chief of the journal:



The screenshot shows the header of the JISSN website. On the left is the JISSN logo with the text "journal of the international society of sports nutrition". To the right of the logo is the text "journal of the international society of sports nutrition" in a larger font. Further right is a yellow box with the text "IMPACT FACTOR 1.91". Below the logo and text is a navigation bar with five buttons: "Home", "Articles", "Authors", "Reviewers", and "About this journal". Below the navigation bar is a paragraph of text: "JISSN focuses on the acute and chronic effects of sports nutrition and supplementation strategies on body composition, physical performance and metabolism." Below this paragraph is a section titled "Editors-in-Chief" with three names and affiliations: "Jose Antonio PhD, NOVA Southeastern University", "Richard Kreider PhD, Texas A&M University", and "Douglas Kalman PhD RD, Miami Research Associates".

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Home Articles Authors Reviewers About this journal

JISSN focuses on the acute and chronic effects of sports nutrition and supplementation strategies on body composition, physical performance and metabolism.

Editors-in-Chief
Jose Antonio PhD, NOVA Southeastern University
Richard Kreider PhD, Texas A&M University
Douglas Kalman PhD RD, Miami Research Associates

Of the two other Editor-in-Chiefs, we find that Dr. Douglas Kalman earned his PhD through a poorly-regarded correspondence college. Moreover, [he was caught](#) changing the protocol of a study to alter the outcome and satisfy a sponsor's financial interest. [The study in question [ignored participants](#) who dropped out due to health complications, then declared the product safe]

And the third Editor-in-Chief, Jose Antonio, has been [mentioned in Sports Illustrated](#) for having his hand in a study that has (minimally) the appearance of impropriety, related to his position in the ISSN held simultaneously with working for a supplement company, and publishing his employer's studies in his own journal:

Even supplement makers that submit their products for independent testing have trouble escaping the appearance of impropriety. In 2008 VPX funded a study by Willoughby on one of its products, a fat burner called Meltdown... That study appeared in the journal of the International Society of Sports Nutrition (ISSN) in December. The CEO of ISSN is Jose Antonio, who had been an employee of VPX for almost a year before the study's publication.

The JISSN has published numerous studies on Creatine nitrate, some of which are funded by their sponsor, MusclePharm, who is not only listed as a sponsor, but who offers grants to ISSN members. Still, at no point have I seen any documentation that suggests the FDA has changed their position on the ingredient. And the Journal of the International Society of Sports Nutrition nonetheless keeps publishing articles on the ingredient, paid for by their sponsor...

That the industry, and MusclePharm in particular, would continue to publish in such a journal is unsurprising. When I examined 25 of their most recent supplement studies, I found that less than 1/3rd (seven total) reported negative results- but of those seven, only two were funded by supplement companies with a vested interest in the outcome. Thirteen studies in my sample were funded by supplement companies, and only two of them reported a negative result—but out of the remaining twelve (unfunded studies) five reported negative findings.

Only 15% of the funded studies I examined in the Journal of The International Society of Sports Nutrition reported a negative finding, while 42% of unfunded studies are negative. Ergo, if a company pays for a study and has a financially vested interest in the outcome, the chance of it showing no results is exponentially lower.

By 2015, Richard Kreider is listed as the author of numerous studies involving Creatine nitrate—but most interestingly, on a study that compared Creatine nitrate to Creatine monohydrate. Of particular note is that while there was a comparison made in the study, the results of the comparison were not made public in the abstract—this obviously looks suspicious, as the study was funded by a company who would lose sales if that information were made public.

Effects of 28 Days of Two Creatine Nitrate Based Dietary Supplements on Body Composition and Exercise Performance in Recreationally Active Males



E Galvan¹, D Walker¹, S Simbo¹, A O'Connor¹, C Goodenough¹, R Dalton¹,
K Levers¹, N Barringer¹, M Cho¹, M Koozehchian¹, F Ayadi¹, Y Jung¹,
C Rasmussen¹, M Greenwood¹, P Murano², C Earnest³ and R Kreider¹

+ Author Affiliations

Abstract

We examined 28d of randomly assigned of (1) Placebo (PL), (2) Creatine (CR, 3 g), (3) Creatine Nitrate (CrN; 1 g CR; 0.5 N) and (4) CrN2X (2 g CR; 1.0 g N) on exercise performance and body composition. Participants (N=48; 21 ±3 y) presented for fasting (12h) testing after abstaining from exercise and alcohol for 48h. Performance (reps at 70% of bench press 1 RM [BP] and repeated sprints on cycle ergometer) was measured at 0 & 4 wks. Body composition (DXA) was measured at 0, 1, & 4 wks. We used GLM to examine mean change (95% CI) from baseline. While all three treatment groups significantly increased BP repetition at 4 wks, total BP lifting volume was greater at 4 wks for CrN2X (294.6 lbs; 95% CI, 196, 393) vs CrN (164.2 lbs; 95% CI, 25, 304) and PL (187.1 lbs; 95% CI, 37, 336, both p=0.02). No treatment effects were observed for cycle ergometry testing (peak or mean power, fatigue slope, and total work). While no difference in fat mass were observed for any treatment group, CrN2X did augment lean mass (1.2 lbs; 95% CI, 0.3, 2.1) and fat-free mass (1.1 lbs; 95% CI, 0.2, 2). Our results indicate that CrN2X can increase muscular endurance, and lean and fat-free mass.

However, my contacts within the industry have told me that this is exactly what the study revealed—i.e. that the far more expensive Creatine nitrate was no better than monohydrate. Financial bias aside, the bigger issue here is why is Dr. Kreider performing studies on an ingredient that the FDA has clearly stated is not proven to be safe, and is not to be sold as a dietary supplement? Unfortunately, Dr. Kreider can't lay claim to ignorance of the regulatory guidelines specific to Creatine, as he has [written extensively](#) on them, and is currently aware of the FDA-rejected status of Creatine nitrate—though he seems to think it's appropriate to test rejected ingredients in human trials:



anthonyroberts @anthonyroberts

7/3/15

@RBKreider @JoseAntonioPhD @jtwheat27
@stout_jeffery After the FDA said not to sell it,
you're testing it on people?

In addition, FDA was unable to establish the safety of your "Creatine Nitrate" based proposed serving levels of "963 mg nitrate per day." For example, you cite "[t]he cu Acceptable Daily Intake (ADI) for nitrate [is] 3.7 mg/kg bw/day (equivalent to 222 n for a 60-kg adult)" in Europe on page 17 and in Japan on page 35 and do not explain of the safety of your higher serving levels. Because the identity of your ingredient is FDA did not attempt to evaluate the safety of the component of your ingredients rela creatine.

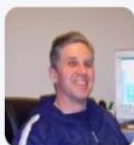
For the reasons discussed above, the information in your notification does not provid adequate basis to conclude that the dietary supplement containing "Creatine Nitrate", used under the conditions recommended or suggested in the labeling of your product, reasonably be expected to be safe. Therefore, your product may be adulterated under U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient fo there is inadequate information to provide reasonable assurance that such ingredient c present a significant or unreasonable risk of illness or injury. Introduction of such a i into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).



Rick Kreider, PhD @RBKreider

7/3/15

@anthonyroberts @JoseAntonioPhD
@jtwheat27 @stout_jeffery. Yes, because its
in lots of supplements and needs to be
studied.



John T Weatherly @jtwheat27

7/3/15

@RBKreider @anthonyroberts
@JoseAntonioPhD @stout_jeffery Good, but
why is MusclePharm selling it if it's not GRAS
and needs FDA to examine?



Rick Kreider, PhD

@RBKreider

@jtwheat27 @anthonyroberts
@JoseAntonioPhD @stout_jeffery Ask
them.

7/3/15, 5:05 PM

1 RETWEET 3 FAVORITES

You'll note that here, Kreider and Antonio- 2/3rds of the JISSN Editor-In-Chief staff—are being made aware that their journal is publishing human trials/studies on FDA-disallowed ingredients. And you'll also note that they don't seem to care—Kreider's answer is to ask their sponsor and not him (the guy actually performing studies).

At this juncture, it's also relevant to ask why Kreider is performing studies on a 2 gram dose, when the patent-holder has claimed a maximum safe dose of 1,570mgs (25% less than the studies have examined)? Were the test subjects made aware (informed consent) of the regulatory status of the ingredient? Did they know that their dose exceeded the manufacturer's maximum?

So I filed a FOI request with Texas A&M

To answer these questions and more, I filed another FOI request, this time with Texas A&M. Their response was to send me a \$12k bill, of which I was required to pay 50% before they got started. Included in this fee is the estimated research time needed on their university mainframe—billed at \$10/minute (ten dollars per minute), and a whopping 353 man-hours—necessary to figure out if they're feeding carcinogens to people in studies, without the people knowing it:

TEXAS A&M UNIVERSITY
Public Information Request #15-601
Requestor Name: Connors
THIS IS AN ESTIMATE ONLY

<i>Resource</i>	<i>Rate per Unit per Public Information Act</i>	<i>Unit</i>	<i>Amount Used</i>	<i>Copies</i>	<i>Total for Resource</i>
CPU:					
Mainframe	\$10.00	minute			
Midsize	\$1.50	minute			
Client/Server	\$2.20	clock hour			
PC or LAN	\$1.00	clock hour			
Programming time*	\$28.50	Hour			
Personnel Charge	\$15.00	hour	353		\$5,295.00
Overhead	20%	Personnel			\$1,059.00
Copies	\$0.10	Page		59622	\$5,962.20
CD	\$1.00	CD/DVD	6		\$6.00
Postage					
				Total Charges:	\$12,322.20
				50% deposit	\$6,161.10

Charges are calculated in accordance with guidelines set forth in the Texas Public Information Act

* The law defines "programming" as "the process of producing a sequence of coded instructions that can be executed by a computer."
 "Manipulation of data" is defined as "the process of modifying, reordering, or decoding of information with human interventions."
 Manipulation of data is not considered programming and would fall under the Personnel charge.

Please make checks payable to: Texas A&M University

Forward payments to: Texas A&M University
 1255 TAMU
 College Station, TX. 77843-1255
 Attn: Tricia Bledsoe or Knesha Brashear

What about Trade Groups?

Right around Springtime, 2015, a series of emails concerning Creatine nitrate and MusclePharm's

ongoing sales of the ingredient, were (*apparently) sent to Steve Mister (smister@crn.org), from the Council for Responsible Nutrition (CRN). As you can see below, numerous trade groups were CC'ed on that email, including The American Herbal Products Association, the Natural Products Association, and more (also, you can see that I was included, along with some other journalists and scientists).

Here is the header from that email chain, along with some of the questions and statements found within:

From: bwkneller@Safe-mail.net <bwkneller@Safe-mail.net>
To: smister@crnusa.org
Cc: ayoung@usatoday.com, mmcguffin@ahpa.org, pcohen@challiance.org, stephen.daniells@wrbm.com, daniel.fabricant@npainfo.org, marc@usulaw.com, anthony@steroids.us.com
Date: Friday, April 03, 2015 01:56 pm
Subject: RE: CRN Support of Criminals that Market Illegal Dietary Supplements

Dear Mr. Mister,

It is a fact that a Vice President of MusclePharm Corp. has a criminal record with a felony conviction for selling misbranded drugs into interstate commerce illegally marketed as dietary supplements. There are multiple "Nitrate salts" currently being sold illegally as dietary supplements. MusclePharm Corp. is a member of CRN and currently sells at least three of these ingredients in as many as seven products. The three ingredients that MusclePharm currently sells are Arginine Nitrate, Creatine Nitrate, and BCAA Nitrate.

The only ndi notification for any "Nitrate salt" that has ever been submitted that I am aware of is for Creatine Nitrate. I am sure you have access to this information and FDA's rejection letter in response to the ndi notification. [The email then goes on to quote and cite the rejection, verbatim] How does CRN support a company that is marketing illegal dietary supplements? How does CRN support a company that is illegally selling products into interstate commerce?

No answers were given to any of these questions...

And not only has CRN done nothing to address their membership selling illegal supplements, but last week, MusclePharm [became a voting member](#) of the trade group. The other trade groups have also chosen to remain silent.

The Wild West?

It's an oft-repeated trope that the supplement industry is the "Wild West," due to a lack of regulation, and that the companies themselves are to blame...but the reality is more sinister. The reality is that the FDA is either lazy or incompetant (or both), the manufacturers (like MusclePharm) are earning too much money to care...and the industry surrounding the manufacturers (i.e. the journals, trade organizations, and scientists), are more than happy to be willing accomplices (or at least pretend they don't know what's going on).

All of these things have allowed a bad ingredient to remain on the market and sell hundreds of

thousands of units, over the course of nearly a decade. People are getting rich giving a likely carcinogen to high-school kids looking to bulk up.

So what happens now?

I don't know.

It's been 1,560 days since Creatine nitrate was rejected by the FDA.

It's been 254 days since my first FOI request was received by them.

The clock is ticking but there's no end in sight.
